EUROPEAN OPHTHALMIC PATHOLOGY SOCIETY

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Location: Basel, Switzerland
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Material Submitted: 1 H&E stained section

Title: Longstanding proptosis and unexpected intra-orbital tumour

Clinical History
An18-year-old female presented with left proptosis for approximately 3years. On clinical examination, she had normal visual function. A 2mm non-axial left proptosis was observed along with some restriction on left adduction. She had no pain or diplopia. Anterior chamber was deep and intraocular pressure within normal limits. On fundoscopy, retina appeared flat and optic disc showed no significant abnormality.

PMH: Attention deficit hyperactivity disorder, anxiety and depression.

MRI and CT scans revealed a left well-defined orbital soft tissue mass in contact with the medial rectus muscle.The lesion measured approximately 18 x 19 x 17 mm (AP x TR x CC) displacingretrobulbar optic nerve inferiorly.Otherwise normal extraocular muscles and tendinous intersections.Post-septal fat was preserved, and there was no inflammatory stranding.No abnormality seen in lacrimal glands,orbitalbones, skull base or intracranially.

A diagnosis of a venous vascular malformation was initially considered. Unfortunately, the patient failed to attend follow up appointments for four years. She then re-presented with similar features reporting no change on her appearance but aware of left exophthalmos. Repeat scans showed no significant interval change.

With a working differential diagnosis of possible cavernous haemangioma or solitary fibrous tumour,an orbital decompression with local excision was planned. A firm,fibrous and vascularised round mass was found via a medial orbitotomy approach. The lesion was displacing medial rectus muscle and optic nerve, being firmly adherent to surrounding tissues. Anterior debulking of the tumourwas performed instead of complete dissection due to increased risk of excessive bleeding and optic nerve injury.

Ophthalmic Pathology
Macroscopy: A pale grey, rubbery, nodular tissue measuring 15 x 12 x 9 mm.

Microscopy: The well-defined mass comprisedfibrous tissue with irregular clusters, nests and interconnecting sheets and trabeculae of round to polygonal cells with abundant eosinophilic, finely granular cytoplasm and round to ovoid, vesicular nuclei with distinct nucleoli. Some cells exhibited patches of dense eosinophilic material within the cytoplasm. Mitotic activity was not conspicuous and there was no necrosis. There was a rich, interconnecting network of capillaries between the cells, and the cell groups were separated by dense fibrous stroma with thick-walled vessels and scattered lymphocytes.Intracytoplasmic elongated, crystalline structures were highlighted with PAS/D stain.Tumour cells expressed TFE3, cyclin D1and cathepsin K.The following markers were negative: CD34, CD31, ERG, STAT6, ALK, D5F3, S100, SOX10, HMB45, MelanA, inhibin, AE1/AE3, SMA, EMA, CD10, BCL2, CD99, synaptophysin, chromogranin, CD56 and CD68. The Ki67 expression was less than 5%. In addition, FISH analysis demonstrated rearrangement of the TFE3 gene, associated with the der(17)t(X;17)(p11.23;q25) translocation.

Diagnosis: Alveolar soft part sarcoma

Discussion
Alveolar soft part sarcoma (ASPS)is a rare sarcoma of uncertain histogenesis characterized by a specific

translocation [der(17)t(X;17)(p11.2;q25)] resulting in *ASPSCR1-TFE3* gene fusion. The tumour was initially described by Christopherson et al. in 1952.There are an average of 6 ASPS cases diagnosed every year in England, making up 0.15% of all soft tissue sarcomas. Although it can present at any age, it is most seen in patients aged 15 - 35 years.There is a 3:1 female preponderance. The main sites involved are deep soft tissues of the extremities (61%), trunk (20%) head and neck (9%) and internal organs(8%). Orbital involvement is mostly seen in children with less than 70 reported cases.

ASPS typically presents asa slow growing, painless mass. Secondary swelling and local symptoms due to compression by the tumour can occur.

CT scan and angiography demonstrate hypervascularity of the tumour with prominent draining veins and prolonged capillary staining. Due to its initial slow growth, reasonably defined contours and vascular architecture, ASPS can mimic arteriovenous malformation onimaging, which might delay a definitive diagnosis.

Diagnostic histological features are eosinophilic polygonal cells with a nested, sometimes organoid growth patternand intracytoplasmic rod-shaped crystals (PAS positive/diastase resistant). Central discohesionmay lead to a pseudoalveolar arrangement. Lobules of tumour are divided by thick fibrous septa and rich capillary vascular network. Cathepsin K is typically positive on immunohistochemistry and TFE3 nuclear expression prompts molecular analysis with confirmation of *TFE3* gene rearrangement (FISH) or *ASPSCR1-TFE3* gene fusion (reverse transcription PCR).Other less common fusion partners with *TFE3* have been identified, including *HNRNPH3-TFE3*, *DVL2-TFE3*and *PRCC-TFE3.*Further less specific markers described are NSE, vimentin and p53.

ASPS is not formally graded but considered to be a high gradetumour. Local recurrence is seen in up to 50% of cases.Although initial course may seem indolent, overall prognosis is poor with development of metastatic disease >10 years after diagnosis. Metastases can involve the lungs, liver, bone and brain. Metastatic involvement of the brain is more common in ASPS than any other sarcoma. Lymph node metastasis is uncommon.

Surgical resection is the treatment of choice, and radiation may reduce the risk of local recurrence. Pre-operative embolisationof orbital tumours has been described to minimise intraoperative bleeding. Adjuvant chemotherapy does not seem to be effective. Excision of lung and brain metastasis may prolong survival.Long term clinical follow up is mandatory given the risk of late metastasis.

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